ABSTRACT OF THE DISCLOSURE

[0169] Acidic amino acid extensions to multimeric proteins, particularly nucleic acid (e.g., DNA or RNA) binding proteins, provide novel acidically modified proteins which can inhibit the function of cellular proteins, thereby regulating and controlling cell growth. The acidically modified nucleic acid binding proteins are engineered to contain a plurality of acidic amino acids appended to the proteins, generally as extensions of the multimerization or dimerization domain at the amino terminus, and can replace the basic region DNA binding domain of a DNA binding protein. The acidically extended nucleic acid binding proteins act as potent dominant negatives which were demonstrated to inhibit the activation of endogenous transactivators, such as AP1. The invention provides novel methods to create such acidically modified DNA binding proteins which can specifically and stably heterodimerize with cellular regulatory proteins and control cell growth. Suitable nucleic acid binding proteins for acidic extensions include members of transcription regulatory protein families, e.g., bZIP and HLH proteins, having characteristic leucine zipper motifs and helix-loop-helix motifs, respectively. The amino terminal extensions of the basic regions of acidically modified nucleic acid binding proteins are comprised of a sequence of amino acid residues, all or some of which are acidic in nature, and produce robust dominant negatives to the native counterpart proteins in the cell. The acidic amino terminal extension affords a unique protein-protein interaction surface and allows stable multimerization or dimerization between a native protein and the acidically extended protein, thereby controlling, via inhibition or inactivation, the functions of cellular protein products of diverse species, including plants, animals, microorganisms, and viruses.